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HAND-DELIVERED

May 24, 2013

Document Processing Desk – FIFRA Section 6(a)(2) Submission
Office of Pesticide Programs
Environmental Protection Agency
Document Processing Room S-4900
One Potomac Yard
2777 S. Crystal Drive
Arlington, VA 22202

re: FIFRA Section 6(a)(2) Submission for Zinc Borate
Potential Toxicity Effects in 28-day Oral Gavage and 7-Day Inhalation Studies
Submitter: U.S. Borax
Product: Borogard ZB, EPA Reg. No. 1624-120

Dear Sir or Madam:

On behalf of the U.S. Borax, I am submitting adverse effect information pursuant to FIFRA Section 6(a)(2) and the implementing regulations in 40 CFR §159 for the active ingredient, zinc borate.

A summary of the adverse effect information is attached. While this information is being submitted in accordance with FIFRA Section 6(a)(2), we believe that the observed toxicity is consistent with the known effects of zinc and zinc compounds.

If you have any questions about this submission, please contact me at (202) 393-3903, ext. 14 or e-mail at eharrison@lewisharrison.com.

Sincerely,

Eliot Harrison
Agent for U.S. Borax

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A 28-Day Oral (Gavage) Dose Range Finding
Toxicity Study of Zinc Borate 2335 in Sprague Dawley Rats

The objective of this study was to evaluate the potential toxicity of zinc borate 2335 when administered daily by oral gavage to Sprague Dawley rats for 28 days to aid in selection of dose levels for a 90-day oral gavage toxicity study. Zinc borate 2335 in the vehicle (1% sodium carboxymethylcellulose) was administered orally by gavage daily for 28 consecutive days to 5 groups of Sprague Dawley rats, 5 animals/sex, with the exception of Group 6 which was dosed for 13 days prior to the early termination, due to mortality and observed toxicity. Dosage levels were 125, 250, 500, 1000, and 2000 mg/kg/day. A concurrent control group received the vehicle on a comparable regimen.

Statistically significant differences in several hematology and serum chemistry parameters were noted in the 250, 500, and 1000 mg/kg/day groups compared to the control group including: erythrogram (lower mean hemoglobin, hematocrit, mean corpuscular volume, and mean corpuscular hemoglobin levels, and higher mean absolute reticulocyte count and red cell distribution width level); leukogram (lower mean absolute white blood cell, lymphocyte, monocyte, eosinophil, basophil, and large unstained cell counts); thrombogram (higher mean platelet volume level); and coagulation parameters (lower mean APTT). Most alterations in the erythrogram, thrombogram, and coagulation parameters were noted only in the 1000 mg/kg/day group, while some leukogram alterations were noted in the 250, 500, and 1000 mg/kg/day group males and in the 500 and 1000 mg/kg/day group females.

Statistically significant differences in serum chemistry parameters included lower mean total protein, albumin, globulin, and cholesterol levels, and higher mean albumin/globulin (A/G) ratio levels. Lower mean total protein and albumin levels were noted in the 250, 500, and 1000 mg/kg/day group males and in the 1000 mg/kg/day group females; lower mean globulin levels were noted in the 500 and 1000 mg/kg/day group males and females; and higher A/G levels were noted in the 250, 500, and 1000 mg/kg/day group females. Lower mean cholesterol levels were noted in the 500 and 1000 mg/kg/day group males and females.

Significant differences in organ weights were noted in the 500 and/or 1000 mg/kg/day groups included lower mean testes, epididymides, ovaries/oviducts, thymus, spleen, and heart weights, and higher mean adrenal gland weights. Lower epididymides weights were noted in the 500 and 1000 mg/kg/day groups, while testes, ovary/oviduct, and spleen weights were lower in the 1000 mg/kg/day groups. Adrenal gland weights were higher and heart weights were lower in the 1000 mg/kg/day group males, and thymus weights were lower in the 500 mg/kg/day group males and the 1000 mg/kg/day group males and females.

Treatment related microscopic findings were noted in the pancreas and glandular stomach in the 250, 500, and 1000 mg/kg/day groups; in the testes, epididymides and kidneys in the 500 and 1000 mg/kg/day groups; and in the seminal vesicles, spleen, and thymus in the 1000 mg/kg/day group at the study day 28 scheduled necropsy.

The low dose of 125 mg/kg/day was determined to be the No Observed Adverse Effect Level (NOAEL).

Seven Day Inhalation Toxicity Study of Zinc Borate 2335 in Rats

The objective of the study was to determine the potential toxicity of zinc borate 2335 when exposed for 6 hours a day/5 days a week for 28 days. However, due to the level of mortality observed after the initial exposures, the study was terminated and exposure period limited to seven days. Zinc borate 2335 was administered via inhalation (nose only) for 5 days over a 7 day period to 5 groups (Groups 2-6) of Sprague Dawley rats. Exposure levels were 250, 500, 750 and 1000 mg/m3 6 hours per day for Groups 2, 3, 4, 5, and 6, respectively. A concurrent control group (Group 1) received filtered air.

Due to the level of mortality observed after the first 2 exposures, exposure to test article was halted for Group 5. Group 5 animals were euthanized for terminal necropsy on Day 5 (females) and 6 (males). Many animals had microscopic evidence of alveolar fibrin and edema consistent with acute lung injury which was suggestive of development of acute respiratory distress syndrome. Group 1-4 animals which survived to terminal necropsy had 5 exposures to test article were euthanized for terminal necropsy on Day 8.

Administration of zinc borate 2335 by nose-only inhalation at an exposure concentration of 500 and 750 mg/m3 for 6 hours per day for 5 days resulted in the early death of 4 and 3 animals, respectively. No mortality was observed in the 250 mg/m3 exposure group.

Of animals surviving to the terminal euthanasia, microscopic findings noted in the lung included: interstitial fibrosis, neutrophilic inflammation, and exudates in the lumen; and nose that included atrophy of olfactory epithelium, degeneration of olfactory epithelium, erosion, neutrophilic inflammation, and squamous metaplasia of olfactory epithelium.